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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/040,791	01/07/2002	Geoffrey N. Roth	MLB0001.01	3954

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EXAMINER	
GITOMER, RALPH J	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 11/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/040,791	ROTH ET AL.	
	Examiner	Art Unit	
	Ralph Gitomer	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *72-83* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *72-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The preliminary amendment received 1/7/2002 has been entered and claims 72-83 are currently pending in this application. This application is a Continuation of 09/357,606 filed 7/20/199, now US Patent 6,350,588. Please update the present specification accordingly. A number of references have been received but no form 1449 is found.

The remarks in the amendment of 1/7/2002 and Declaration by Roth regarding Aeromonas reacting with glucuronide as described by Sartory are found convincing and the reference is not applied here.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 72-80 are directed to a selective medium to detect, quantify and differentiate coliforms, E. coli and one of Aeromonas, Salmonella and in claim 76 Shigella, wherein the medium comprises ions of a salt, a beta-glucuronic non-chromogenic substrate which reacts in the presence of E. coli to form a black color, a second chromogenic substrate which reacts in the presence of coliforms to form a second color, and a third chromogenic substrate which reacts in the presence of Aeromonas, Shigella or Salmonella to form a third color. Claims 81-83 are method claims utilizing the above medium which are considered separately here.

Claims 72-75, 77-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Roth in view of James and further in view of each of Monget and Perry.

Roth (5,726,031) entitled "Test Media and Quantitative Method for Identification and Differentiation of Biological Materials in a Test Sample" teaches a medium for detecting, quantifying and differentiating coliforms, E. coli and Salmonella, wherein the medium comprises ions, an inhibitor of non-enterobacteriaceae, and chromogenic beta-glucuronic and beta-galactosidic substrates. In column 5 last full paragraph, line 56 particularly, a medium is disclosed that distinguishes non-coliform Enterobacteriaceae, Salmonella and Shigella. Roth further teaches that galactoside substrate may be 6-Cl-beta-gal in column 12 lines 30-39, and teaches that a 5-Br-4-Cl-indolyl linked, (i.e. blue)

chromogenic substrate may combine with a 6-Cl-3-indolyl (i.e. red) substrate to form a different color, purple, which can be distinguished from the color of either chromogen along in column 9 line 64 bridging to column 10 line 7.

Roth differs from the claims in that the claims specify 8-hydroxyquinoline as a beta-glucuronide substrate specifically and a chromogenic substrate that reacts with Salmonella or Aeromonas.

James (Zbl. Bakr. Hyg.) entitled "Detection of Specific Bacterial Enzymes by High Contrast Metal Chelate Formation: Specific Detection of E. coli on Multipoint Inoculated Plates Using 8-Hydroxyquinoline-Beta-D-Glucuronide" teaches 8-hydroxyquinoline-beta-D-glucuronide which reacts in the presence of E. coli and a ferric salt to give black pigmentation in the summary. This substrate may be used in place of fluorescent and chromogenic substrates, and teaches that the hydroxyquinoline substrate does not react with Shigella strains which react with other beta-glucuronic substrates, on page 320.

Roth in view of James renders obvious a medium comprising ferric ions, an inhibitor, a chromogenic beta-galactoside substrate, and 8-hydroxyquinoline-beta-D-glucuronide.

The claims differ from James in that they specify a chromogenic substrate for Aeromonas or Salmonella and a galactoside.

Monget (4,308,348) entitled "Test for Bacteria" teaches a variety of chromogenic aliphatic ester substrates for detecting and distinguishing Salmonella from other

microorganisms, including E. coli and other coliforms in column 4 lines 20-68. Monget teaches that Salmonella substrates may be combined with other substrates, including those for galactosidases and glucuronidase in column 3 lines 14-20, and teaches that such substrates may comprise either chromogenic or fluorescent moieties, or may comprise hydroxyquinoline in column 3 lines 3-9. Monget specifically teaches that substrates should be combined with others in a single medium in column 3 lines 10-13.

Perry (WO 98/55644) entitled "Identification of Salmonella" teaches 5-Br-4-Cl-3-indolyl-alpha-D-galactoside (X-alpha-gal) for detecting Salmonella in a mixed sample, and teaches that X-alpha-gal may be combined with a beta-galactoside substrate in a medium on page 12. Further, other coliforms, including E. coli, produce alpha-galactosidase on page 2, thus suggesting that X-alpha-gal is a substrate for general coliforms as well as for Salmonella. Perry also teaches that Salmonella does not produce beta-galactosidase on page 2, thus suggesting that Salmonella would not react with a beta-galactoside substrate.

It would have been obvious to one of ordinary skill in the art at the time of the invention to have included the X-alpha-gal of Perry in the medium of Roth and James where the motivation would have been to facilitate detection and differentiation of Salmonella in a mixed culture or sample, as taught by both Roth and Perry. One skilled in the art would reasonably have expected that the X-alpha-gal of Perry would react with coliforms as well as with Salmonella, as suggested by Perry's teaching that coliforms reduce alpha-galactosidase. Based on the teachings of Roth that coliforms react with 6-Cl-3-indolyl-beta-galactoside to form a red color, that X-linked chromogens form blue

and that a reaction for a microorganism with both forms purple, and the suggestion of Perry that coliforms can react with X-alpha-gal, one skilled in the art would reasonably have expected the purple color to be distinguishable from a blue color produced in the presence of Salmonella. To clarify, one skilled in the art would reasonably have expected coliforms to react with both the alpha-gal (blue) and beta-gal (red) substrates to form purple, as suggested by Roth, while Salmonella as taught by Perry would be expected to react with alpha-gal substrates only, to form blue. E. coli would reasonably be expected to react with all substrates, but would be distinguished by the black precipitate formed by reactions with the hydroxyquinoline glucuronide substrate and ferric ions, as taught by James. One skilled in the art would reasonably have expected success in combining the substrates of Roth, James, and Perry because Roth and Perry teach that beta-glucuronidase and alpha-galactosidase substrates can be combined with beta-galactosidase substrates, James teaches that his substrate and ferric ions can be used in place of chromogenic substrates, and all teach that their substrates can be used in media for detection and differentiation of E. coli from other microorganisms.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the 8-hydroxyquinoline-beta-D-glucuronide and ferric salt of James for the chromogenic glucuronide in the medium of Roth where the motivation would have been to use a substrate which is specific for E. coli and does not cross-react with Shigella, as taught by James. It would further have been obvious to have included the chromogenic aliphatic ester substrates of Monget in the medium of

Roth and James where the motivation would have been to detect and distinguish Salmonella from E. coli and other coliforms in a single medium as taught by both Roth and Monget. Inclusion of the substrate of Monget would have been an improvement in the medium of Roth and James because Monget teaches that esterase substrates are specific for Salmonella and Serratia, and would thus facilitate use of the medium for identification and differentiation of Salmonella vs. E. coli and other coliforms. One skilled in the art would reasonably have expected success in combining the substrates of Roth, James and Monget in a single medium to detect and distinguish E. coli, coliforms and Salmonella because both Roth and Monget teach that galactoside and glucuronide substrates may be combined in a medium, Monget teaches that hydroxyquinoline linked substrate can be used in place of chromogenic beta-glucuronide substrates, and Monget teaches that esterase substrates can be combined with other substrates, specifically with a galactoside, and can be used to distinguish Salmonella, E. coli and other coliforms.

Claim 76 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Roth in view of James and further in view of each of Monget and Perry as applied to claims 72-75, 77-83 above, and further in view of Kampfer.

The teachings of Roth, James, Monget and Perry are disclosed above.

Claim 76 differs from the above references in that it includes a substrate to distinguish Shigella specifically.

Kampfer (J of Clinical Microbiol) entitled "Glucosidase Profiles of Members of the Family Enterobacteriacea" teaches that various Enterobacteriaceae can be distinguished using chromogenic substrates, and specifically teaches that Shigella species react with a fluorogenic alpha-galactosidase substrate but not with a beta-galactosidase on page 2878 Table IV.

It would have been obvious to one of ordinary skill in this art to employ the substrate taught by Kampfer with the substrates of the primary references because Kampfer shows the presently claimed substrate is known for detecting Shigella.

To combine different and specific indicators in a single selective medium to facilitate detection, quantification, and differentiation of different and specific microorganisms is old in this art. To employ known indicators for their known function with the expected results would have been obvious. No unexpected results of the presently claimed combination of indicators is disclosed.

Claims 81-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Townsend in view of Monget.

Townsend (WO 96/40980) entitled "Method and Composition for Detecting Bacterial Contamination in Food Products" teaches on page 5 line 8, ferric chloride. On page 6 lines 10-13, bacterial enzymes detecting include beta-D-galactosidase and beta-D-glucuronidase. On page 7 line 14, color and fluorescent emission are shown as detectable signals. On page 8, three or more different bacterial enzymes may be measured. On page 8 last paragraph, various bacteria are listed including Aeromonas

spp, E. coli and on page 9 first paragraph, coliforms. Two or more bacteria may be detected. On page 13 last paragraph, a glucuronide indicator changes to blue when E. coli is present.

See claim 3 on page 27 directed to detecting or measuring the concentration of Aeromonas, coliforms, and E. coli. A number of galactoside and glucuronide indicators are listed in Table 1.

The claims differ from Townsend in that they specify Salmonella is detected, and 8-hydroxyquinoline is employed for detecting Shigella in claim 83.

Monget (4,308,348) entitled "Test for Bacteria" teaches a variety of chromogenic aliphatic ester substrates for detecting and distinguishing Salmonella from other microorganisms, including E. coli and other coliforms in column 4 lines 20-68. Monget teaches that Salmonella substrates may be combined with other substrates, including those for galactosidases and glucuronidase in column 3 lines 14-20, and teaches that such substrates may comprise either chromogenic or fluorescent moieties, or may comprise hydroxyquinoline in column 3 lines 3-9. Monget specifically teaches that substrates should be combined with others in a single medium in column 3 lines 10-13.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to detect any desired additional microorganism in the method of Townsend, such as Salmonella, by the method of Monget because Townsend teaches detecting any desired microorganism by combining known indicators for detecting microorganisms and Monget specifically teaches detecting Salmonella with the same

substrate as claimed. To employ known substrate indicators for their known function with the expected results would have been obvious.

Claims 72-83 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for hydroxyquinoline-beta-D-glucuronide, does not reasonably provide enablement for any nonchromogenic beta-glucuronide substrate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

The claims are directed to a selective medium and associated method with at least three substrates but the substrates are not defined in the claims to permit one of skill in this art to make and use the invention.

The claims are not enabled for distinguishing Shigella from E. Coli and coliforms because neither the specification nor the prior art teach how to distinguish organisms which all react with beta-glucuronic substrates using a medium comprising a nonchromogenic substrate other than hydroxyquinoline-beta-D-glucuronide which produces a black color in the presence of beta-glucuronidase. The specification provides guidance in Table IV (p. 27) that E. coli is positive for beta-glucuronidase whereas Salmonella/Shigella are negative for beta-glucuronidase. Although they are different organisms, the specification does not provide guidance for enzyme activity in Salmonella and Shigella separately. In contrast to the guidance of the specification, the prior art provides guidance that 100% of Shigella sonnie and over 30% of Shigella

species react with chromogenic beta-glucuronidase substrates, see Kampfer p. 2878; J Clinical Microbiol 1991 29(12)2877-2879. The prior art also teaches that beta-glucuronidase genes are found in all Shigella species tested, and teaches that at least 70% of each of three different species of Shigella react with a fluorogenic beta-glucuronidase substrate, see McDaniels p. 3351, Table 1, Appl Environ Microbiol 1996 62(9)3350-3354., thus suggesting that Shigella will react with a beta-glucuronide substrate in the instant medium. As both Shigella and E. coli are beta-glucuronidase positive, both would be expected to react with a nonchromogenic beta-glucuronide substrate in the instant medium to produce a black color. As the black color would be expected to cover or mask any other color produced by chromogenic substrates, one skilled in the art would conclude that it would be difficult or impossible to distinguish Shigella from E. coli using a medium comprising an nonchromogenic beta-glucuronic substrate. The prior art of James confirms that Shigella reacts with beta-D-glucuronidase substrates, but also provides guidance for a particular substrate, hydroxyquinoline-beta-D-glucuronide, which reacts with E. coli to form a black color, but which does not react with at least two strains of Shigella known to react with chromogenic and fluorogenic beta-D-glucuronide substrates, see James p. 320, Zbl. Bakt. Hyg. A 1988, Vol. 267, pp. 316-321. There is no guidance in the prior art for whether this difference is found for differential reactions of E. coli and Shigella with any other nonchromogenic beta-glucuronidase substrate. The level of skill in the art is acknowledged to be high. However, given the degree of uncertainty for whether Shigella can be distinguished from E. coli by reaction with a beta-glucuronidase

substrate other than the hydroxyquinoline-beta-D-glucuronide taught by James, it would require undue experimentation for one skilled in the art to determine how to use a medium comprising any nonchromogenic glucuronide substrate other than hydroxyquinoline-beta-D-glucuronide to distinguish E. coli, coliforms, and Shigella. For these reasons, the claims are enabled for a medium comprising hydroxyquinoline-beta-D-glucuronide for detection and differentiation of E. coli, coliforms and Shigella, but are not enabled for a medium comprising any other nonchromogenic glucuronic substrate which forms a black color, for the same intended purpose.

Further, the specification is enabling for a method to detect and distinguish E. coli, coliforms, and Salmonella, wherein the medium comprises a nonchromogenic beta-glucuronic substrate which forms a black color, but does not reasonably provide enablement for a similar medium for detecting and distinguishing E. coli, coliforms and Aeromonas. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. See above regarding enablement for distinguishing E. coli, coliforms and Shigella.

Regarding the claims directed to a selective medium and method for distinguishing Aeromonas from E. coli and Salmonella and other organisms, using a medium comprising a nonchromogenic beta-glucuronide substrate which forms a black precipitate, the claims are enabled for a medium to distinguish E. coli, Salmonella and coliforms because the instant specification teaches how to do so and the prior art supports the guidance of the specification. The claims are not enabled for a medium

and method to distinguish Aeromonas from E. coli wherein the medium comprises a nonchromogenic beta-glucuronide substrate which forms a black precipitate or color because it would require undue experimentation to determine whether Aeromonas can be distinguished from E. coli using such a medium. The instant specification provides guidance on page 27, Table IV that Aeromonas and Salmonella/Shigella do not produce beta-glucuronidase. As set forth above, the specification does not provide guidance for enzyme activity of Salmonella and Shigella separately. The prior art of Kampfer provides guidance that one species of Salmonella reacts with a beta-glucuronide substrate, but that only 4% of total isolates of Salmonella species do so. One skilled in the art would therefor expect to be able to distinguish most Salmonella species from E. coli using the instantly claimed medium but unable to distinguish coliforms and E. coli from Aeromonas using the claimed medium and method. The level of skill in the art is acknowledged to be high, however, given the uncertainty engendered by the different teachings of the specification and the prior art, it would require undue experimentation for one skill in the art to determine how to distinguish Aeromonas from E. coli and coliforms using a medium comprising a nonchromogenic beta-glucuronide substrate which produces a black precipitate or color. For these reasons, the claims are enabled for distinguishing E. coli, coliforms and Salmonella using a medium comprising a nonchromogenic beta-glucuronide substrate, but are not enabled for distinguishing Aeromonas, E. coli and coliforms using the same medium.

Claims 74 and 76 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of the following applies in all occurrences.

In claim 74 line 2, "one of" appears redundant because only one genus is recited. In claim 74 last line, "nonenterobacteriaceae" is queried because it does not appear to be a term of art. In claim 76 "substantially nondiffusible" is not defined by the claim or the specification.

The title of the invention is not aptly descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following prior art pertinent to applicant's disclosure is made of record and not relied upon:
Roth (6,350,588) is the parent application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ralph Gitomer whose telephone number is (703) 308-0732. The examiner can normally be reached on Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (703) 308-1235. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Ralph Gitomer
Primary Examiner
Art Unit 1651

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